**NOTE:** This guidance was prepared in the event that highly pathogenic avian influenza (H5N1) is introduced into the United States through returning travelers or poultry. In the event of introduction, this guidance is expected to change rapidly. Make certain you are operating from the most current guidance posted

at: <a href="http://www.wvidep.org/AZIndexofInfectiousDiseases/Influenza/tabid/1518/Default.aspx">http://www.wvidep.org/AZIndexofInfectiousDiseases/Influenza/tabid/1518/Default.aspx</a>
These guidelines are for providers, laboratories and local health departments. For state-level health department responsibilities, see Appendix 3.

## **Provider Responsibilities**

- Report suspect cases of avian influenza to the local health department immediately.
   Diagnosis of avian influenza should be considered in a patient with influenza-like illness or pneumonia and:
  - a. Travel to a country with H5N1 outbreaks; and history of :
    - i. Direct contact with domestic poultry;
    - ii. Consumption of uncooked poultry or poultry products;
    - iii. Direct contact with poultry feces; OR
    - iv. Close contact with a known or suspected human case of H5N1.
  - History of close contact with an ill patient who was confirmed or suspected to have H5N1; OR
  - c. Occupational exposure to live influenza H5N1 in a laboratory. Consult IDEP (800-423-1271) or the local health department to determine if testing should be performed. Testing decisions will be made on a case-by-case basis depending on the current case definition and the situation. Testing for avian influenza can be performed free-of charge.
- 2. If a suspect case of avian influenza is identified:
  - a. Immediately <u>isolate the patient</u> using standard, airborne and contact precautions (Source: OSHA):
    - i. For hospitalized patients, notify infection control at the earliest possible time, certainly before a suspect patient is admitted or transferred.
    - ii. Use fit-tested N-95 masks, gloves and gowns for health care workers with direct patient contact;
    - iii. Eye protection for health care workers within 3 feet of the patient;
    - iv. Negative pressure isolation for the patient;
    - v. Pay close attention to hand hygiene after all interactions with the patient; and
    - vi. Minimize patient transport or movement within or between healthcare facilities. If the patient must be moved use the most practical measures to contain patient secretions (if possible, place a surgical mask on the patient).

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- b. Assist in confirmation of the diagnosis by supplying clinical information as requested and laboratory specimens to rule out or confirm the diagnosis.
- c. If the patient is a strong suspect, initiate treatment with neuraminidase inhibitors, according to standard recommendations. WHO suggests 150 mg oseltamivir BID X 10 days. (See New England Journal of Medicine, 2008; 358:261-273.)
- d. Assist state and local public health personnel in identifying close contacts (unprotected face-to-face contact within 3 feet) of the patient.

### **Laboratory Responsibilities**

1. Urgently refer all requests for testing for avian influenza to the Infectious Disease Epidemiology Program at 304-558-5358 or 800-423-1271.

#### **Public Health Action**

- Educate local providers and laboratories about reporting requirements (above). Maintain capability to transmit health alerts to local providers when requested by the state health department.
- 2. Take steps to protect employee health, as follows:
  - a. Vaccination for seasonal influenza is offered to employees on an annual basis; and
  - b. Fit-tested N-95 masks or better protection should be available to personnel for case and outbreak investigation. Gowns and gloves should be available, if contact with respiratory secretions is likely.
  - c. Goggles or eye protection are available for personnel who will be within 3 feet of the patient.
- 3. If a <u>suspect case of highly pathogenic avian influenza</u> (see case definition) is reported, take all of the following steps:
  - a. Assure the suspect case is appropriately isolated using airborne and contact precautions.
  - b. Complete the 'Human A (H5) Domestic Case Screening Form.' FAX to IDEP at 304-558-8736.
  - c. Begin a line listing of contacts using "Form 2B: Avian Influenza Primary Contact/Site Worksheet." Contacts are defined as persons who came within 3 feet of the patient from one day prior to onset of symptoms through 7 days after resolution of fever (or up to 21 days). Using form 2B, prioritize the list of contacts, and identify which contacts are high priority (priority 1-3). Complete "Form 2D: Avian Influenza Contact Tracing Form" for each high-priority contact.

- d. Assist health care providers and IDEP in obtaining laboratory studies for confirmation.
- e. If highly pathogenic avian influenza is confirmed:
  - i. Assure the patient remains in isolation through at least 7 days after resolution of fever, or up to 21 days.
  - ii. Notify IDEP. Complete the screening form, and attach copies of all laboratory slips and a copy of the chest radiograph report. FAX the completed forms to IDEP at 304-558-8736.
  - iii. Begin oseltamivir prophylaxis on close contacts (75 mg daily for 7 to 10 days).
    - 1. Doses for children ≥ 1 year of age:
      - a. 30 mg QD for < 15 kg
      - b. 45 mg QD for > 15 to 23 kg
      - c. 60 mg QD for > 23 to 40 kg
      - d. 75 mg QD for > 40 kg
    - 2. No recommendation is available for children < 1 year of age
  - iv. Educate contacts about:
    - 1. Transmission of avian influenza:
    - 2. Cough etiquette;
    - 3. Self-referral to medical care if symptoms develop. The patient should be educated to contact the health care facility by phone prior to traveling to a health care facility so that health care providers can take appropriate precautions.
  - v. Arrange to talk to contacts daily by phone for 7 days after last exposure, if resources allow. Passive surveillance of contacts is also acceptable. Document daily contact on "Form 2E: Avian Influenza Contact Surveillance Form."
  - vi. If a contact becomes ill with fever, refer the contact for medical care immediately. Notify the health care facility so health care personnel can take precautions. Notify IDEP immediately so arrangements can be made for laboratory confirmation.
  - vii. Alert other providers in the county through the local health alert network to be watchful for additional human cases.
- 4. If a <u>suspect or confirmed human exposure to highly pathogenic avian influenza (H5N1)</u> is reported, e.g., exposure from an agricultural or environmental source.
  - a. Suspect/confirmed exposure includes:
    - Direct contact with sick or dead wild or domestic birds suspected or confirmed to have influenza H5N1;
    - ii. Ingestion of undercooked meat or blood from infected birds; or
    - iii. Direct contact with feces from infected birds.

- b. Management of exposed persons:
  - i. Begin oseltamivir prophylaxis (75 mg daily for 7 to 10 days).
  - ii. Ask exposed persons to remain under surveillance for 7 days after last exposure.
  - iii. Educate exposed persons about:
    - 1. Infection control procedures at home (hand washing, bag household trash and dispose in the usual way, clean the household in the usual way with ordinary household cleaners);
    - Transmission of avian influenza;
    - 3. Cough etiquette;
    - 4. Self-referral to medical care if symptoms develop. The patient should be educated to contact the health care facility by phone prior to traveling to a health care facility so that health care providers can take appropriate precautions.
  - iv. If resources allow, arrange to talk to exposed persons daily by phone until seven days have passed after last exposure. Passive surveillance of exposed persons is also acceptable if resources are limited. Document daily contact on "Form 2E: Avian Influenza Contact Surveillance Form."
  - v. If the exposed person becomes ill with fever, refer him/her for medical care immediately. Notify the health care facility so health care personnel can take precautions. Notify IDEP immediately so arrangements can be made for laboratory confirmation.

### **Disease Control Objective**

If a case of avian influenza is identified, prevent person-to-person spread by:

- a. Isolation of the index case;
- b. Identification, surveillance and prophylaxis of contacts.

### **Public Health Significance**

In recent years, massive epidemics of 'bird flu' (avian influenza) have captured media attention and raised concerns about a worldwide pandemic of H5N1 influenza. From initial reports of poultry and human disease in Hong Kong in 1997, the virus has been identified in over 50 countries in Europe, Asia, Africa and the Middle East. The virus has evolved from a single strain to include at least 10 clades (numbered 0 to 9). Clades vary in sensitivity to antiviral agents. The majority of clade 1 viruses are resistant to amantadine and rimantidine; but the majority of clade 2 viruses are sensitive. All viruses are susceptible to neuraminidase inhibitors, but variations in susceptibility have been

reported. There are also implications for vaccine development: vaccine-induced immunity may be specific to clade type. If avian influenza arrives in the United States, prevention and treatment recommendations will have to be formulated according to the strain of virus imported into the country.

As we enter the 2008-2009 influenza season, 385 human cases, including 243 deaths have been reported worldwide. Most human cases and deaths have occurred in association with exposure to poultry. So far, spread from one human to another has only been identified in a few family clusters. In these family units, prolonged, close exposure has been documented; however a genetic predisposition to efficient person-to-person spread cannot be excluded.

The major concern surrounding this new virus is the possibility that the virus may change to a form that is efficiently transmitted from one person to another, thereby precipitating the next influenza pandemic.

This protocol was developed in response to this concern and is designed towards an aggressive containment strategy if one or a few cases of human H5N1 were documented in our state. If a larger number of cases were reported or if human-to-human transmission becomes highly efficient, resources would be insufficient for containment and investigators should refer to pandemic influenza guidance (Appendix 2).

For current case counts and information on avian influenza, see: http://www.who.int/csr/disease/avian\_influenza/en/index.html

## **Clinical Description:**

Symptoms in patients with <u>avian influenza</u> have included: high fever and influenza-like illness with lower respiratory tract symptoms. Other symptoms have included diarrhea, vomiting, abdominal pain, pleuritic pain, and bleeding from the nose and gums. Patients have also presented with encephalitis. Dyspnea may develop approximately 5 days into illness, followed by respiratory distress, tachypnea, and inspiratory crackles. Sputum production is variable and sometimes contains blood.

The hallmark of disease is viral pneumonia progressing to acute respiratory distress syndrome. Case fatality rate is about 60%. Median time to hospitalization is 4 days. Median time from onset to death is 9 days. Case fatality rate is highest in children and declines with age. Mildly symptomatic illness has not been documented by serosurveys of populations in close contact with sick and dying poultry; however mild upper respiratory illness has been documented in children in several cluster investigations since 2005.

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Optimal treatments for avian influenza in humans remain to be discovered; however, most experts recommend early initiation of oseltamivir (within 48 hours of onset). Optimal dose and duration are unknown. WHO suggests using oseltamivir at twice the usual dose and duration: 150 mg BID X 10 days. Some consideration should be given to combination of neraminidase inhibitors with adamantanes, if the strain is likely to be susceptible to both agents. See New England Journal of Medicine, 2008; 358:261-273. Mortality remains high in spite of therapy.

### **Etiologic agent**

A continually evolving avian strain of influenza A. The virus has evolved into several distinct clades and subclades, each with a different geographic distribution. Viruses from clades and subclades 0, 1, 2.1, 2.2, 2.3 and 7 have caused human disease.

While other avian influenza viruses have caused human disease, this protocol refers specifically to highly pathogenic influenza A (H5N1). A brief catalogue of human disease cause by interspecies transmission of avian influenza viruses is found in the table below:

Year	Antigenic description and interspecies transmission event
Pre-1997	H1N1, 1918 Spanish flu epidemic?
	H7N7, sporadic conjunctivitis
1997	H5N1 in Hong Kong, 18 cases and 6 deaths
1998, 1999, 2003	H9N2 in Hong Kong and Guangdong (mild flu-like illness)
2003	H5N1 diagnosed in Hong Kong (likely acquired in Fujian Province, People's
	Republic of China) and in mainland China
2003	H7N3 in Holland; 89 laboratory-confirmed cases; 83 of 85 patients presented
	with conjunctivitis and 5 of these also had flu-like illness. A veterinarian
	developed pneumonia, multi-organ failure and death.
2004	H7N3 in Canada; conjunctivitis and flu-like illness
2004 – present	H5N1 disease and death in southeast and east Asia, central Asia, the Middle
	East, and Africa

### Reservoir

Avian influenza viruses (H5N1) appear to be maintained in poultry and dissemination is primarily related to movement of poultry and poultry products. Migratory wild birds may spread the virus to new geographic locations. A large outbreak resulted in the death of over 6,000 migratory waterfowl in Qinghai Lake in western China in 2005. Subsequently, wild bird outbreaks were reported elsewhere in Asia and the Middle East. Ducks can be infected without manifesting symptoms and

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are hypothesized as a 'Trojan horse,' freely visiting backyard flocks and silently introducing the virus to susceptible populations of poultry. Spillover hosts include domestic cats, tigers and leopards, which have become infected after feeding on infected poultry.

#### **Mode of Transmission**

Direct avian-to-human transmission is the most common mode of transmission. Handling sick or dead poultry during the week before onset, slaughtering, defeathering, preparing sick or dead poultry for cooking, and consuming raw or undercooked poultry or poultry products have all been implicated in transmission. Clusters of human illness suggesting person-to-person spread have occurred in close family units suggesting either intense exposure or genetic predisposition or both. In one quarter of patients, the source of exposure is unclear, and environment-to-human transmission remains possible.

WHO suggests that "respiratory secretions and all bodily fluids, including feces, should be considered potentially infectious."

Drinking potable water or properly cooked foods are not considered risk factors. Ingestion of virus-contaminated products or swimming in contaminated water might pose a risk. (WHO)

### Incubation period

For avian influenza, the incubation period has generally been in the range of 2-4 days, with an upper limit of 7 days (WHO).

### Infectious period

For avian influenza, use an infectious period of 1 day before to 14 days after onset of symptoms (WHO).

## Interim Case Definition for Suspected H5N1 Cases in the U.S.

Testir	ng for avian influenza A (H5N1) virus is recommended for a patient who:
	Has an illness that requires hospitalization or is fatal; <b>and</b>
	Has or had a documented temperature of ≥ 38 °C (≥ 100.4 °F); <b>and</b>
	Has radiographically confirmed pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternate diagnosis has not been established; and

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- Has at least one of the following potential exposures within 10 days of symptom onset:
  - a. History of travel to a country with influenza H5N1 documented in poultry, wild birds and/or humans **and** had at least one of the following potential exposures during travel:
    - Direct contact with (e.g., touching) sick or dead domestic poultry;
    - Direct contact with surfaces contaminated with poultry feces;
    - Consumption of raw or incompletely cooked poultry or poultry products;
    - Direct contact with sick or dead wild birds suspected or confirmed to have influenza H5N1;
    - Close contact (approach within 1 meter [approx 3 feet]) of a person who was hospitalized or died due to a severe unexplained respiratory illness;
  - b. Close contact (approach within 1 meter [approx 3 feet]) of an ill patient who was confirmed or suspected to have H5N1;
  - c. Worked with live influenza H5N1 virus in a laboratory.

Persons with mild or atypical disease or persons with unknown or uncertain epidemiological information may be considered for testing on a case-by-case basis. Consult the Infectious Disease Epidemiology Program at 304-558-5358 or 800-423-1271

## Interim Case Definition for use in association with an H5N1 outbreak in poultry in the U.S.

The case and contact classifications outlined below have been developed as preliminary guidance for use in the event of an avian influenza A (H5N1) outbreak in U.S. domestic poultry and should be adapted, as necessary, for the specific outbreak conditions. This guidance is based on the current state of knowledge regarding human infection with influenza A (H5N1) viruses; however, it may be modified for use during poultry outbreaks caused by other notifiable avian influenza viruses. As of this writing, influenza H5N1 has not been identified among animals or humans in the United States. In addition, no sustained human-to-human transmission of influenza H5N1 has been documented anywhere in the world, consistent with WHO Pandemic Phase 3 (Pandemic Alert Period). This guidance will be updated as our knowledge of the epidemiology of influenza H5N1 changes.

Cases are classified as follows:

#### A suspect case is a person who:

 Has had a documented temperature of ≥38°C (≥100.4°F) and at least one following symptoms - cough, sore throat, and/or respiratory distress.

and

Has had one of the following exposures within 10 days of the first symptom:

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- Direct contact with (e.g., touching) sick or dead domestic poultry
- Direct contact with surfaces contaminated with poultry feces
- Consumption of raw or incompletely cooked poultry or poultry products, including blood
- Close contact (within 3 feet) of an ill patient who was confirmed or suspected to have H5N1 influenza
- Works with live H5N1 influenza virus in a laboratory.

#### and

- Has a laboratory test for H5N1 that is pending, inadequate, or unavailable.
  - Examples might include persons who died prior to testing or for whom testing can not be done, and persons with a positive result for influenza A by rapid antigen testing alone;

#### A **confirmed case** is a person who:

Meets the clinical and exposure criteria for a Suspect Case (see above)

#### and

- Has a positive test for H5N1 influenza by one or more of the following methods:
  - o Isolation of an H5N1 influenza virus by viral culture
  - Positive reverse transcriptase–polymerase chain reaction (RT-PCR) for H5N1
  - Positive immunofluorescence antibody test for H5 antigen, using H5N1 monoclonal antibodies
  - 4-fold rise in H5N1-specific antibody titer detected by microneutralization assay in paired serum samples

Note: If a person tests positive by any of the methods above, but does not meet the clinical and exposure criteria, they may still be counted a confirmed H5N1 infections and treated as a confirmed case for the purpose of the investigation and follow-up.

#### A report under investigation is a person who

 Does not fulfill the suspect case criteria, in terms of exposure or clinical characteristics because information is not yet available. Additional information is needed to classify into one of the other case classifications.

#### Not a case

 Negative for H5N1 influenza as determined by sensitive laboratory testing methods with adequate and appropriately timed specimens.

### **Laboratory Diagnosis of Avian Influenza**

The Office of Laboratory Services offers PCR testing at no cost for both seasonal influenza and circulating avian strains. Results are shared by fax or phone. Appropriate specimens for testing for influenza include:

- Broncheoalveolar lavage specimens
- Tracheal aspirates
- Throat Swab
- Sputum
- Nasopharyngeal or oropharyngeal aspirates, washes, or swabs
- Viral Culture

Consult the Infectious Disease Epidemiology Program at (304) 558-5358 if testing is needed.

## **Preventive Interventions:**

The strategy in this protocol is based on the hope that aggressive, early containment of H5N1 will prevent the spread to human populations. The key to this strategy is:

- Early recognition, isolation and treatment of human suspect and confirmed cases; and
- Early quarantine and prophylaxis of close contacts.

Vaccines are under investigation.

#### **Surveillance indicators**

- 1. Time to reporting of the index case.
- 2. Number of contacts identified per case.
- 3. Proportion of cases with complete information.